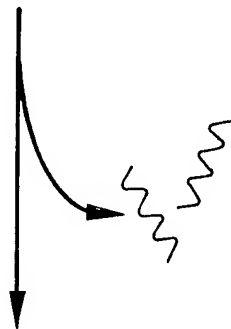


COLUMN CHROMATOGRAPHY

1. EXCHANGE pH 4.0 CITRATE FOR pH 7.5 HBS
2. NEUTRALIZE SURFACE DODAP; ANTISENSE RELEASE
3. REMOVAL OF NON-ENCAPSULATED ANTISENSE



RELEASE OF
SURFACE
ANTISENSE

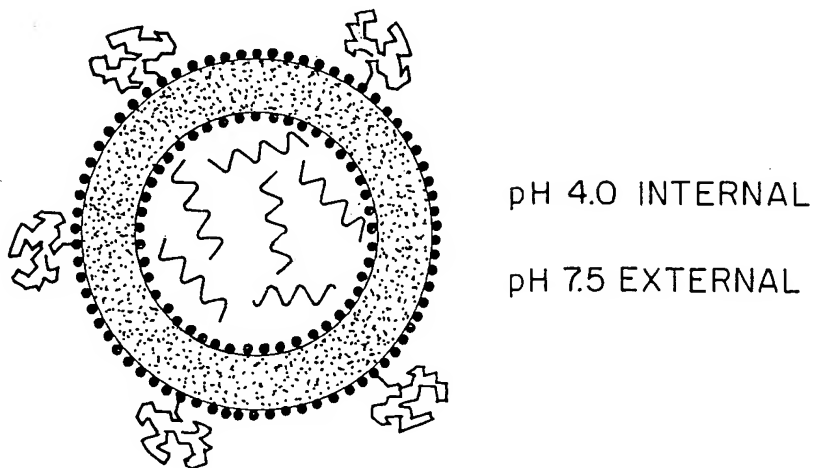
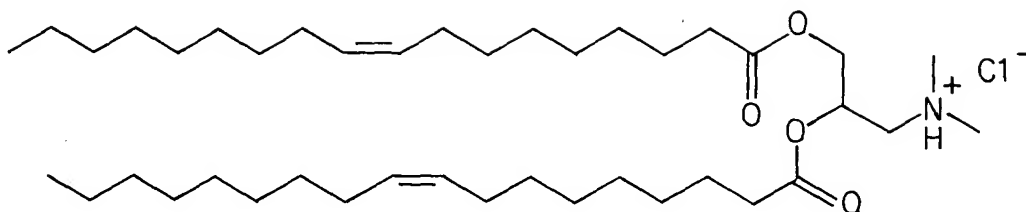
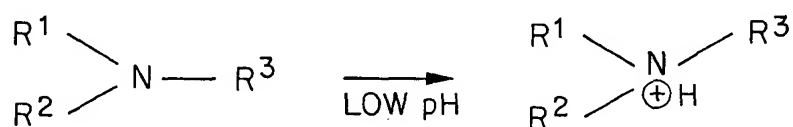


FIG. 1

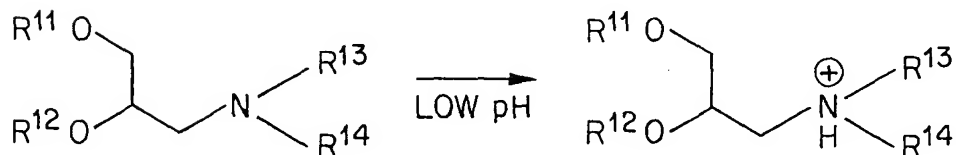
DODAP: AL-1



OTHER AMINO LIPIDS:



R^1 AND/OR R^2 ARE H,
ALKYL OR FATTY ALKYL GROUPS
 R^3 IS H, LOWER ALKYL.



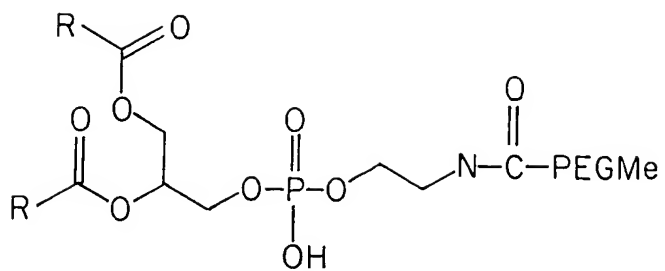
R^{11} AND/OR R^{12} ARE LOWER ALKYL / LOWER ACYL, FATTY ALKYL,
FATTY ACYL.

(AT LEAST ONE OF R^{11} OR R^{12} IS A LONG CHAIN ALKYL OR ACYL
GROUP)

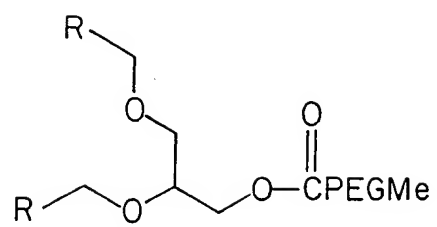
R^{13} AND R^{14} ARE EACH H, LOWER ALKYL.

FIG. 2A

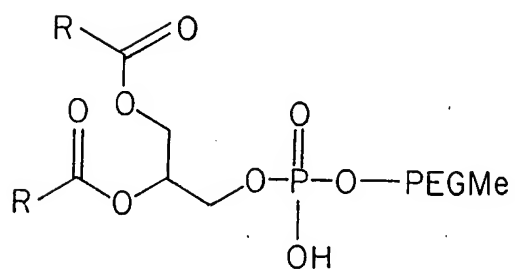
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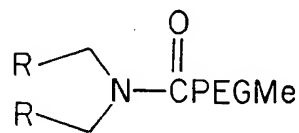
A



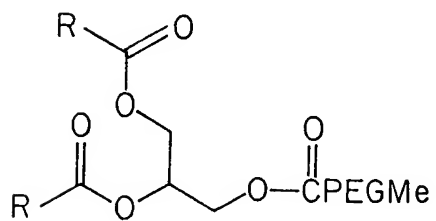
D



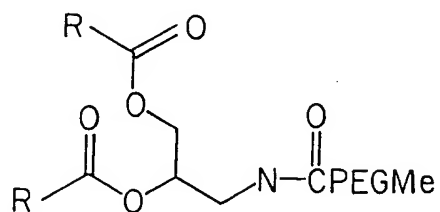
B



E



C



F

FIG. 2B

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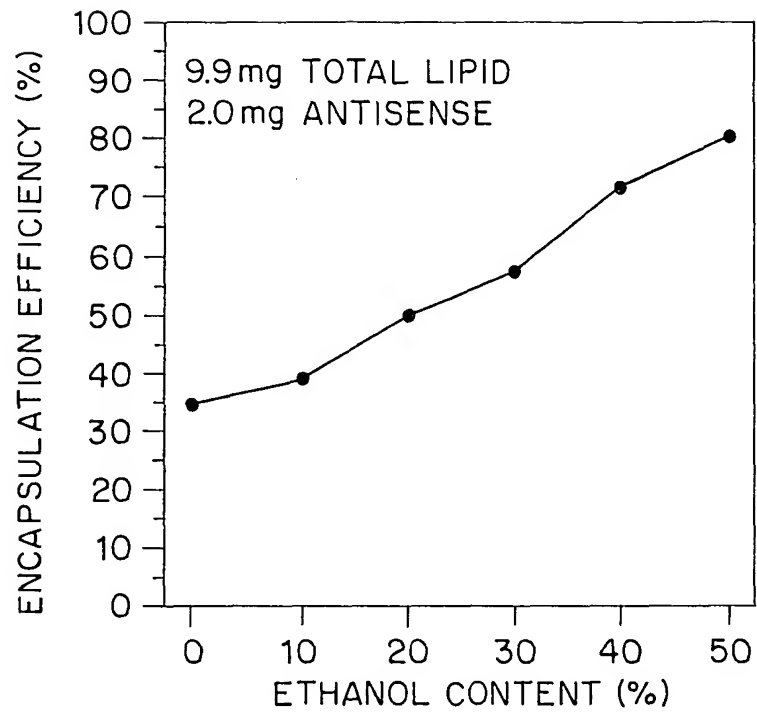


FIG. 3

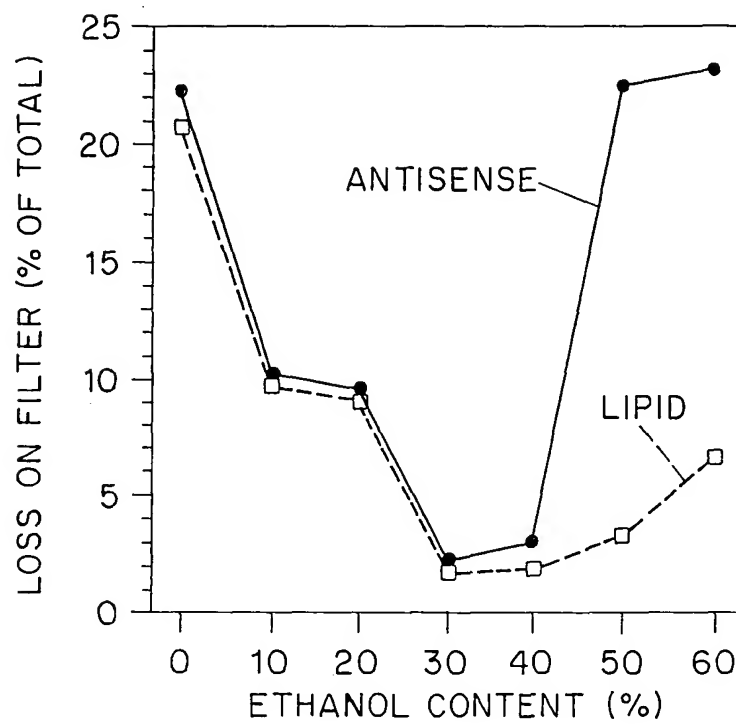


FIG. 4

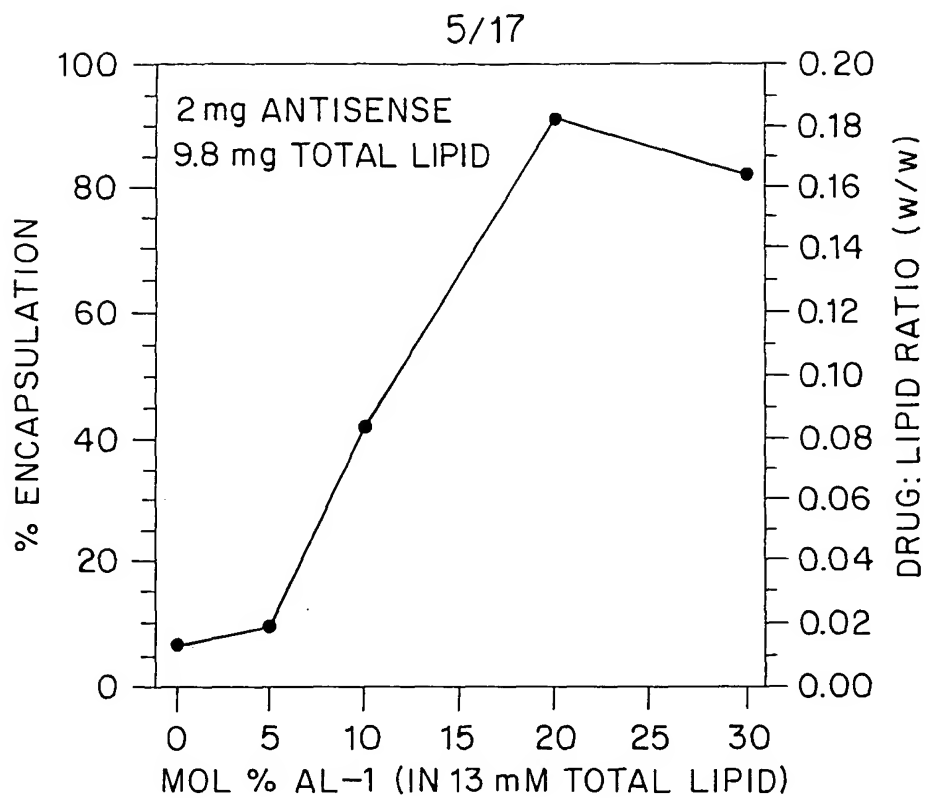


FIG. 5

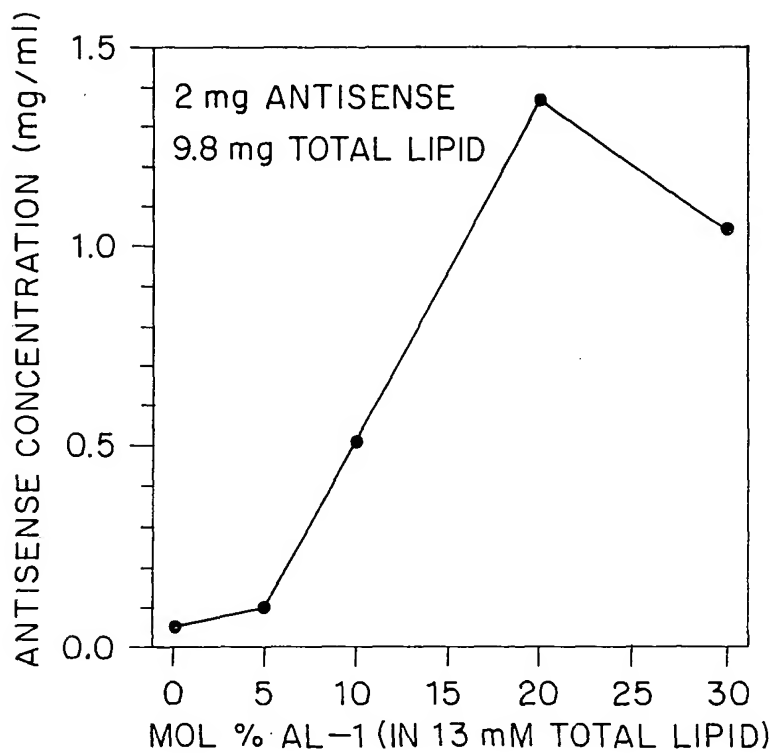
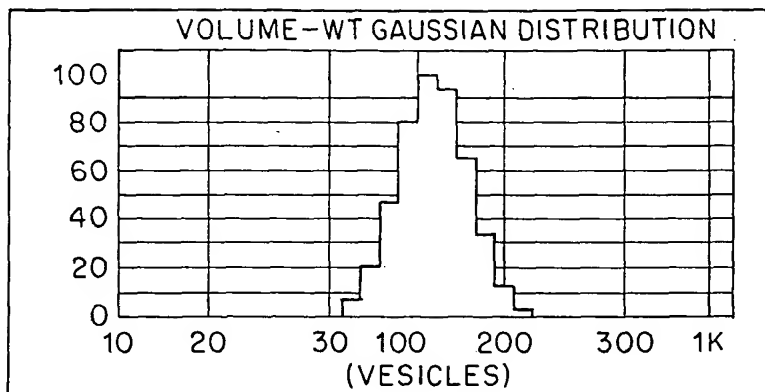


FIG. 6

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IMMEDIATELY AFTER REMOVAL OF FREE ANTISENSE



VOLUME WEIGHTING:

MEAN DIAMETER = 119.3 nm

STD DEVIATION = 32.2 nm (27.0 %)

CUMULATIVE RESULTS:

25 % OF DISTRIBUTION < 88.60 nm

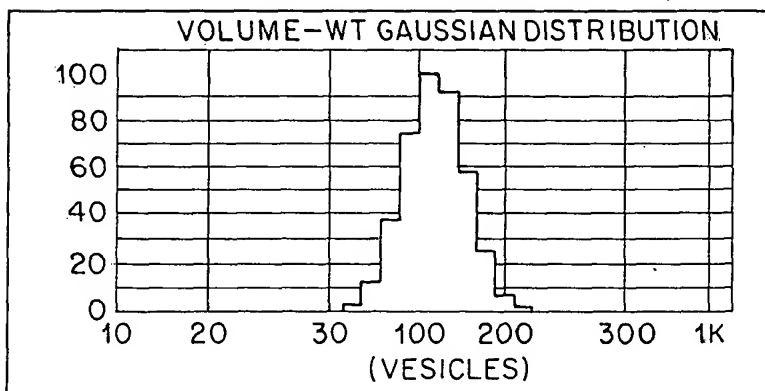
50 % OF DISTRIBUTION < 106.74 nm

75 % OF DISTRIBUTION < 127.93 nm

90 % OF DISTRIBUTION < 151.04 nm

99 % OF DISTRIBUTION < 199.22 nm

AFTER 2 MONTH STORAGE AT 4°C



VOLUME WEIGHTING:

MEAN DIAMETER = 114.2 nm

STD DEVIATION = 27.8 nm (24.3 %)

CUMULATIVE RESULTS:

25 % OF DISTRIBUTION < 86.96 nm

50 % OF DISTRIBUTION < 102.86 nm

75 % OF DISTRIBUTION < 121.31 nm

90 % OF DISTRIBUTION < 140.78 nm

99 % OF DISTRIBUTION < 183.74 nm

FIG. 7

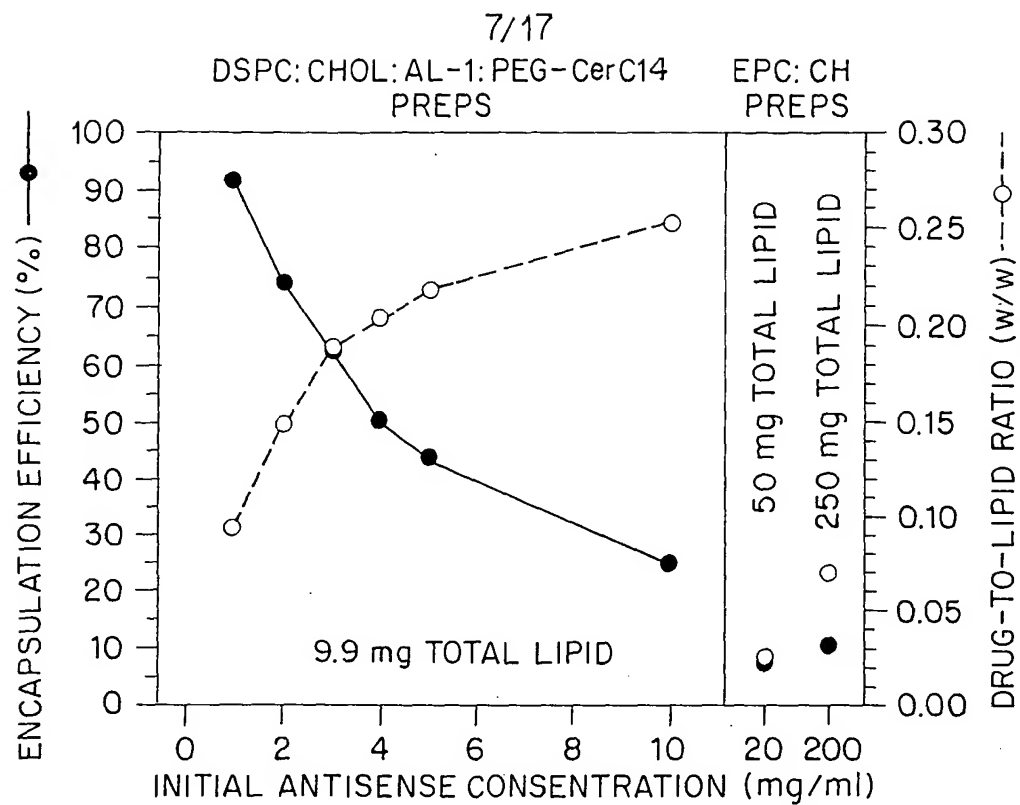


FIG. 8

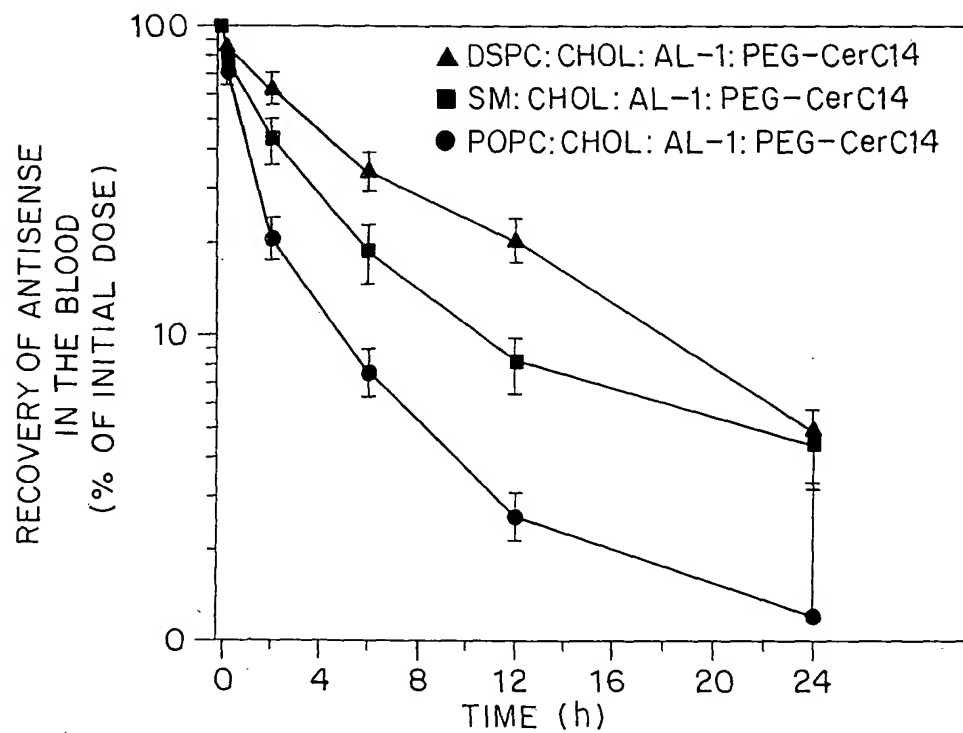


FIG. 9

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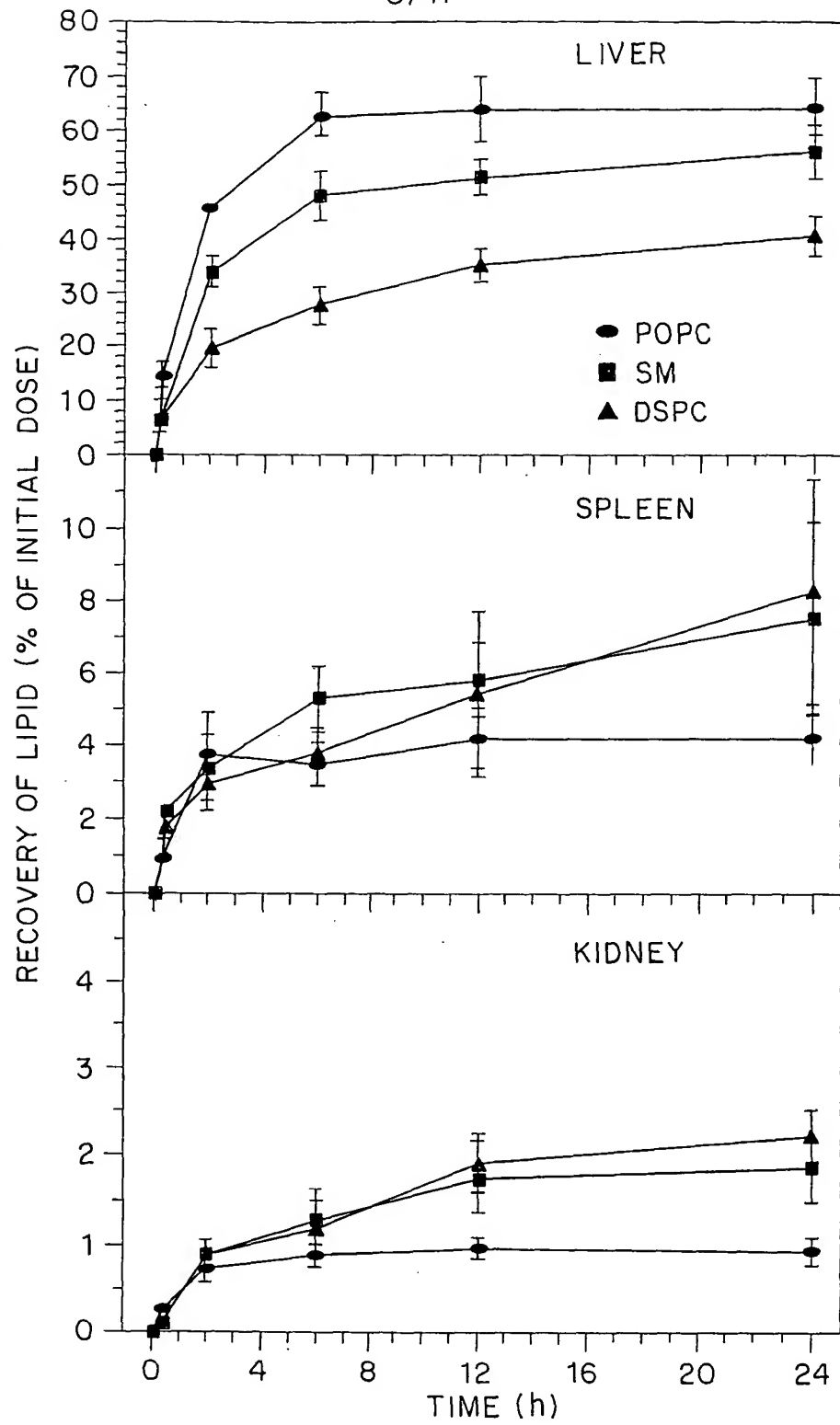


FIG. 10

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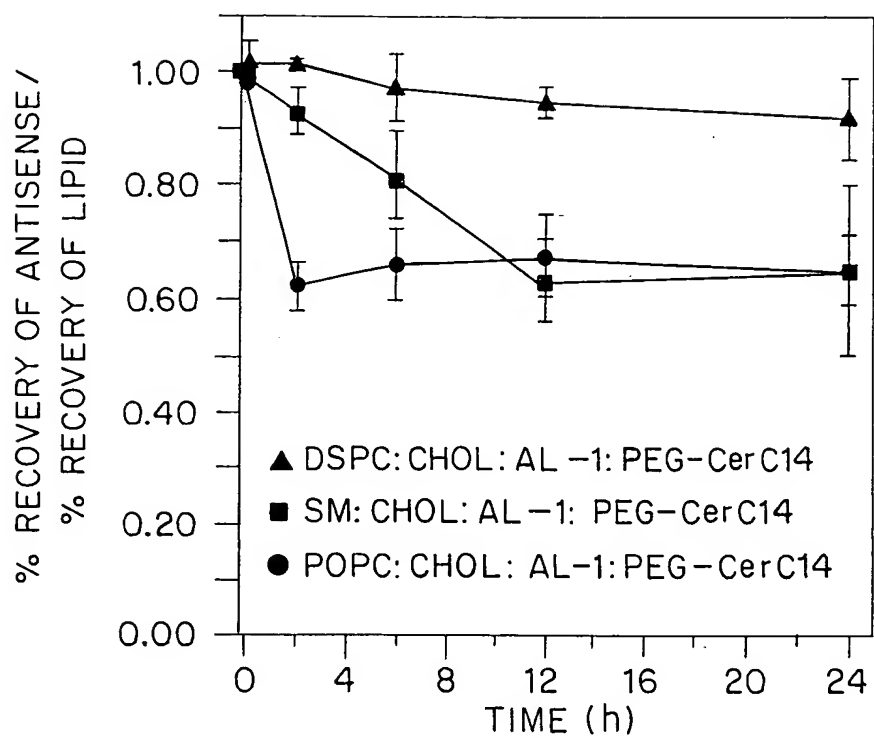


FIG. 11

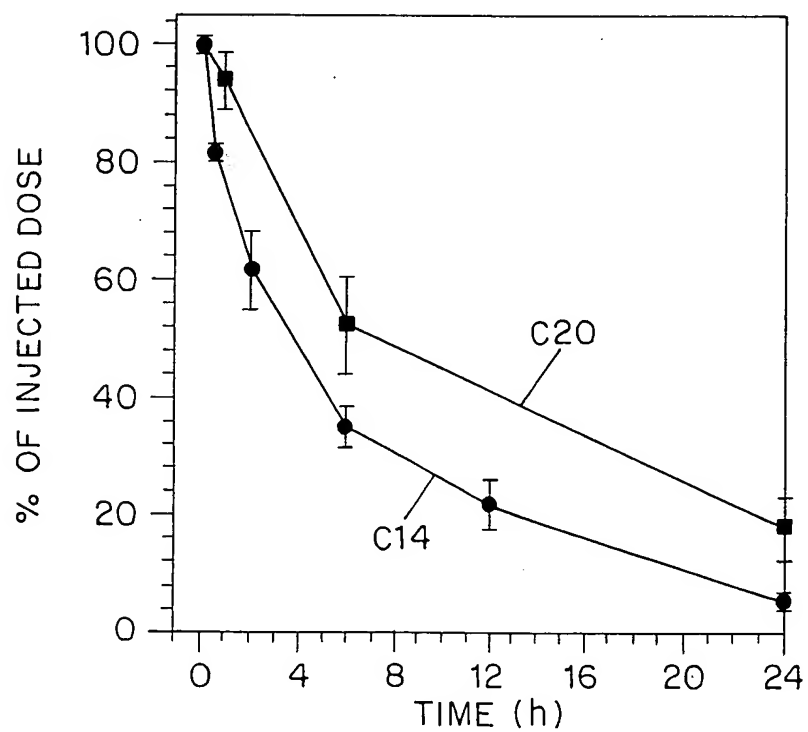


FIG. 12

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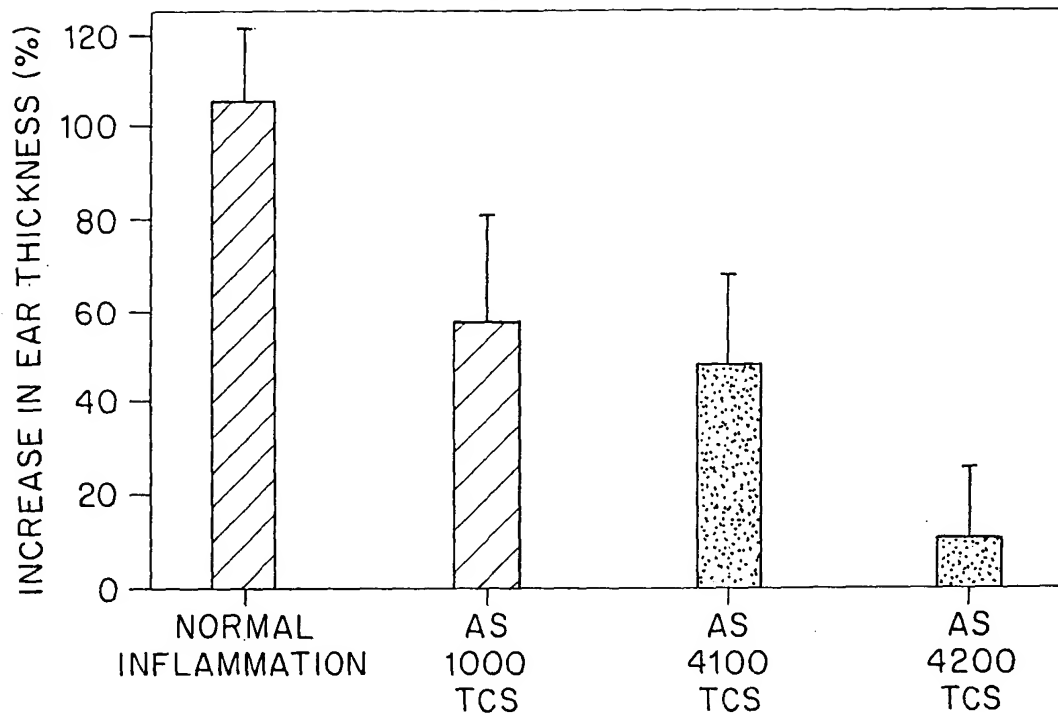


FIG. 13

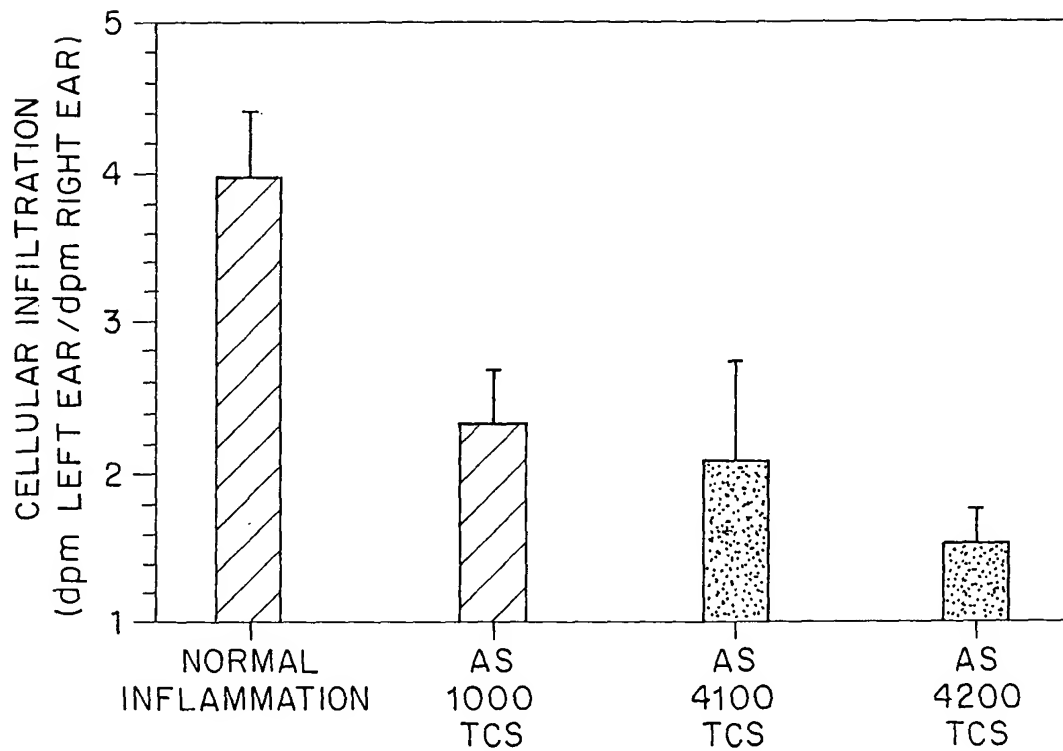


FIG. 14

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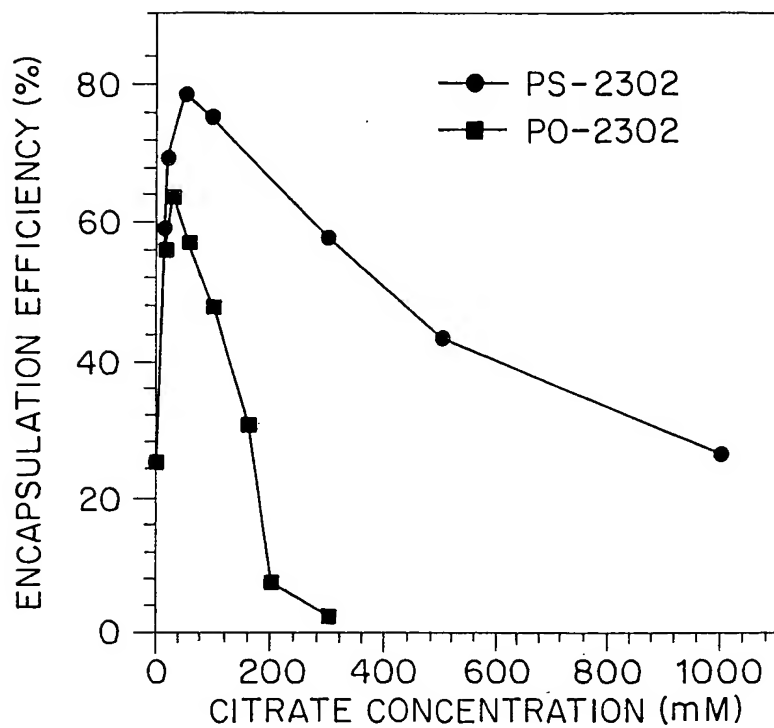


FIG. 15

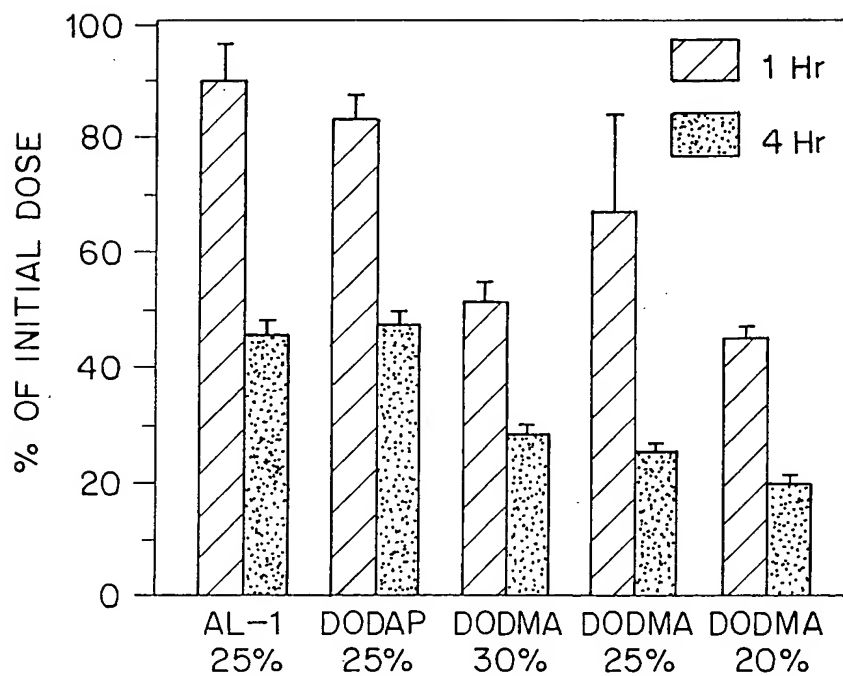
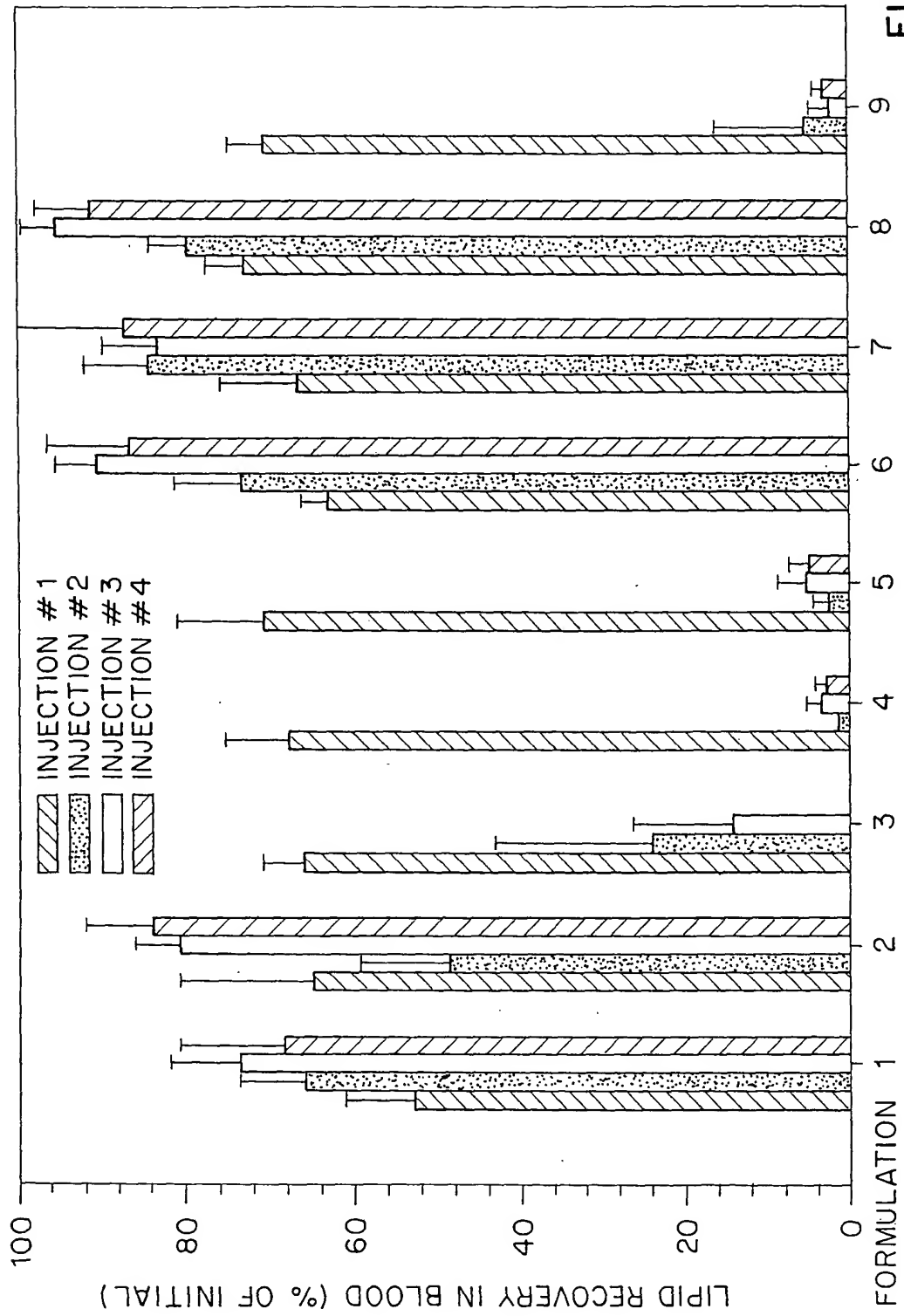


FIG. 16

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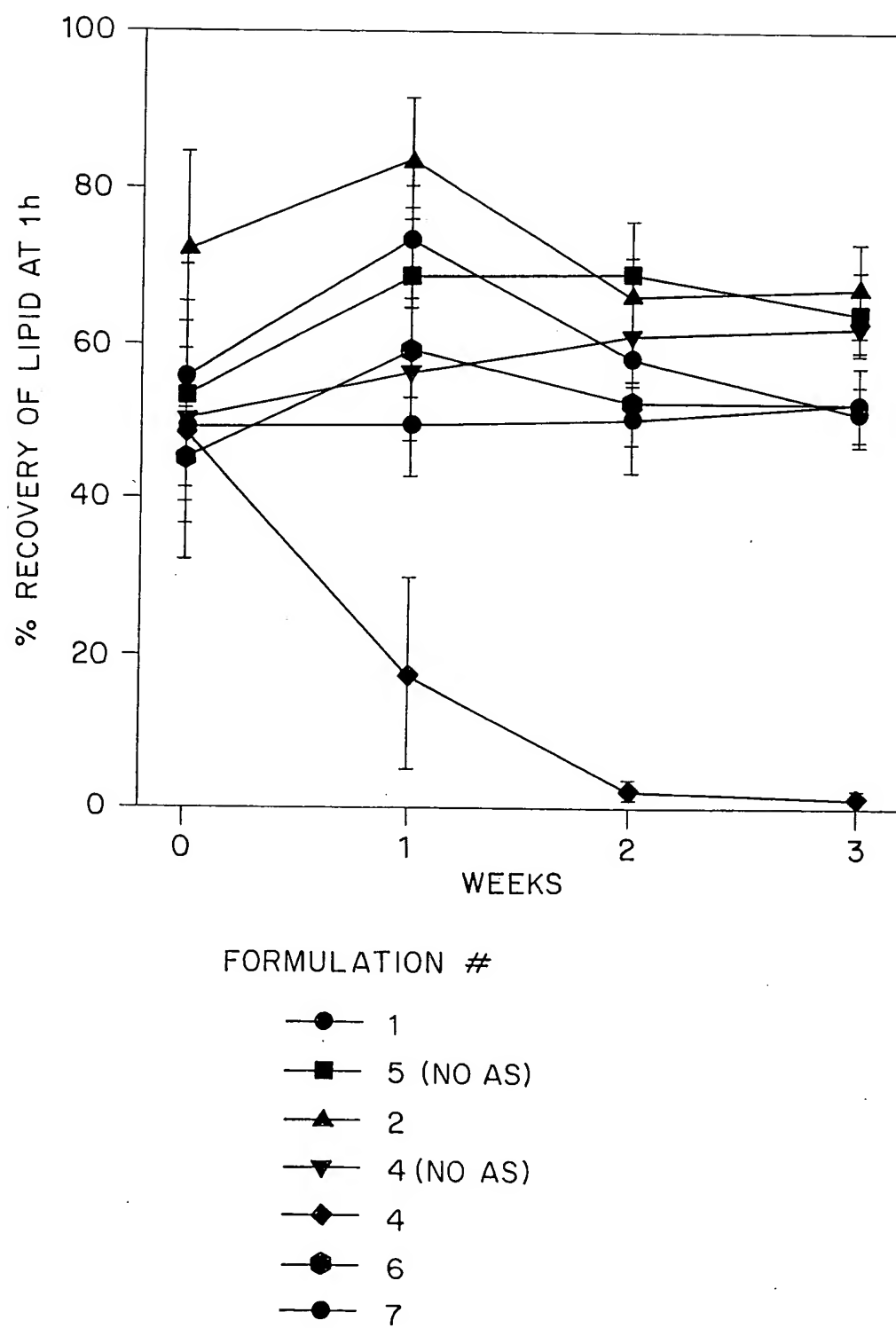


FIG. 18

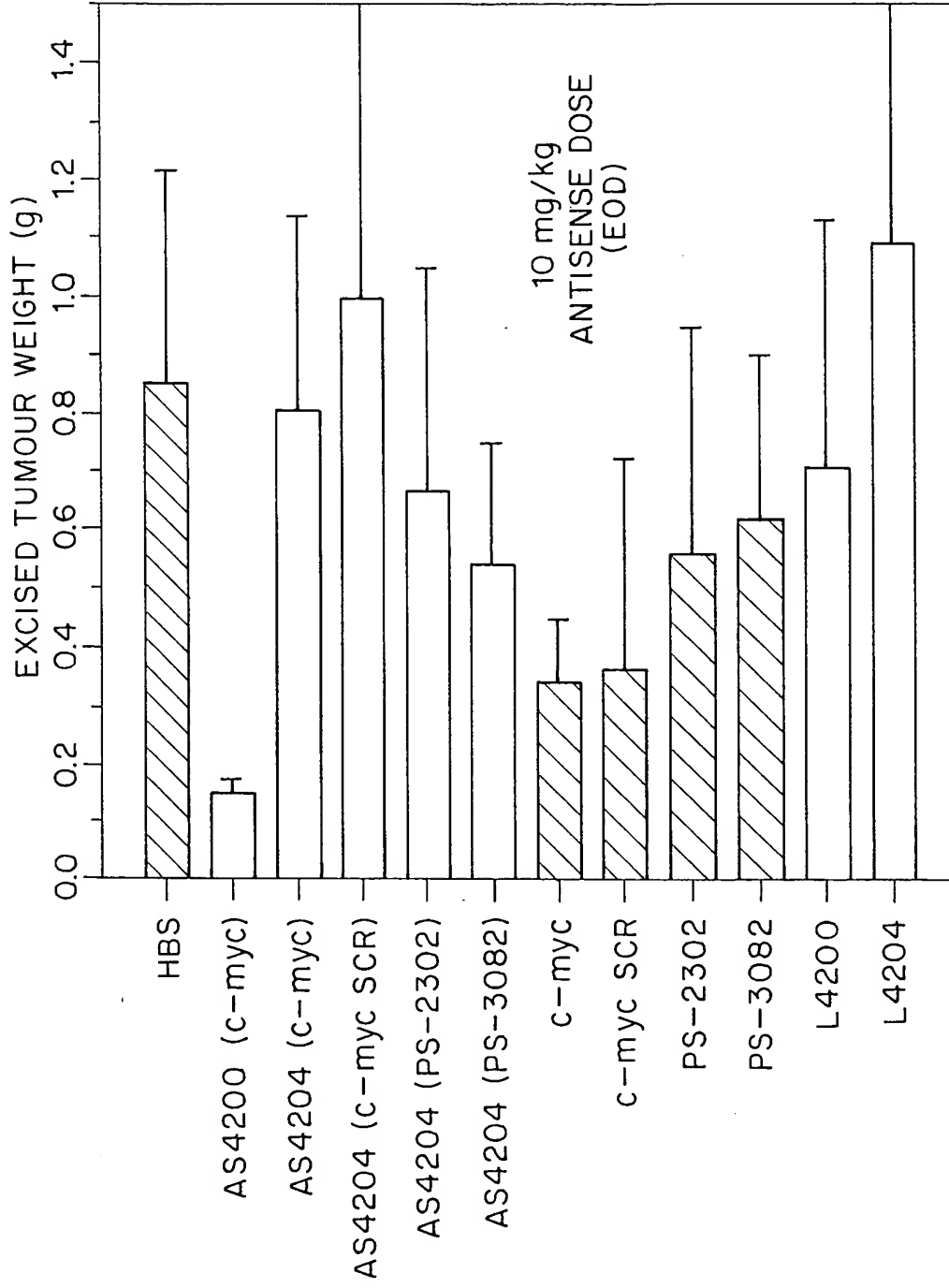


FIG. 19

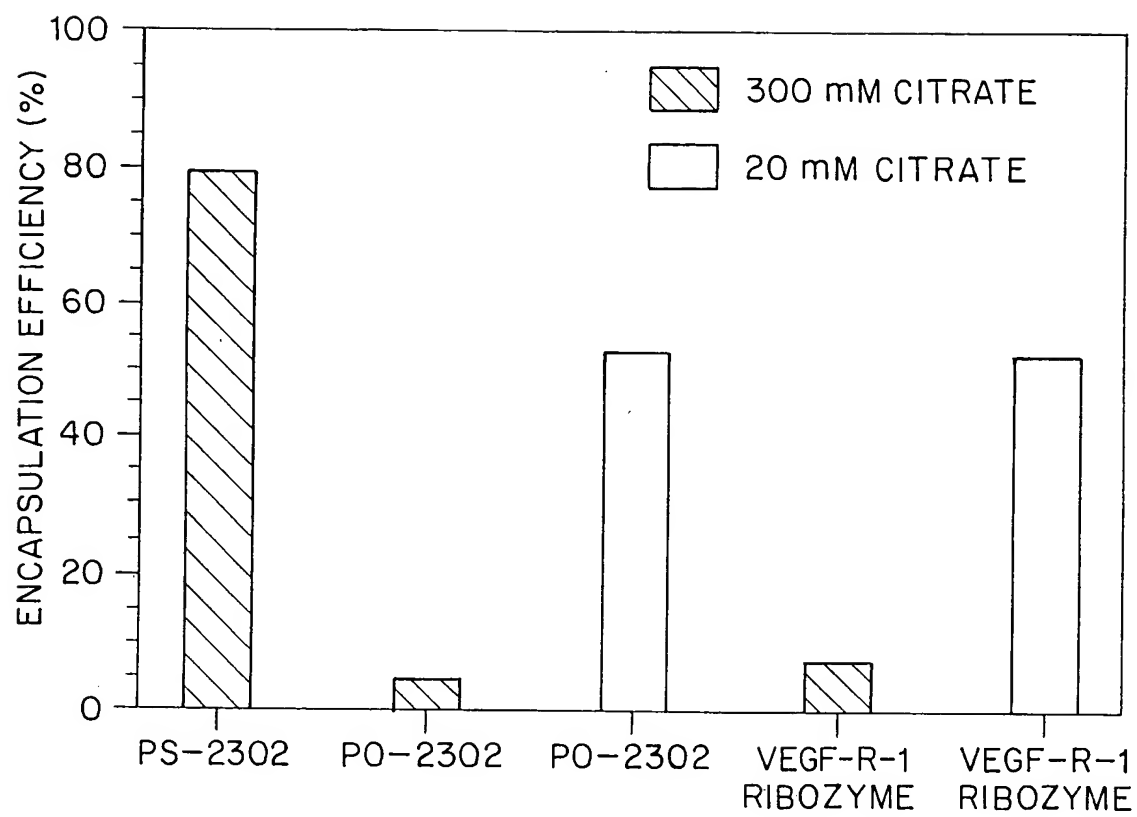


FIG. 20

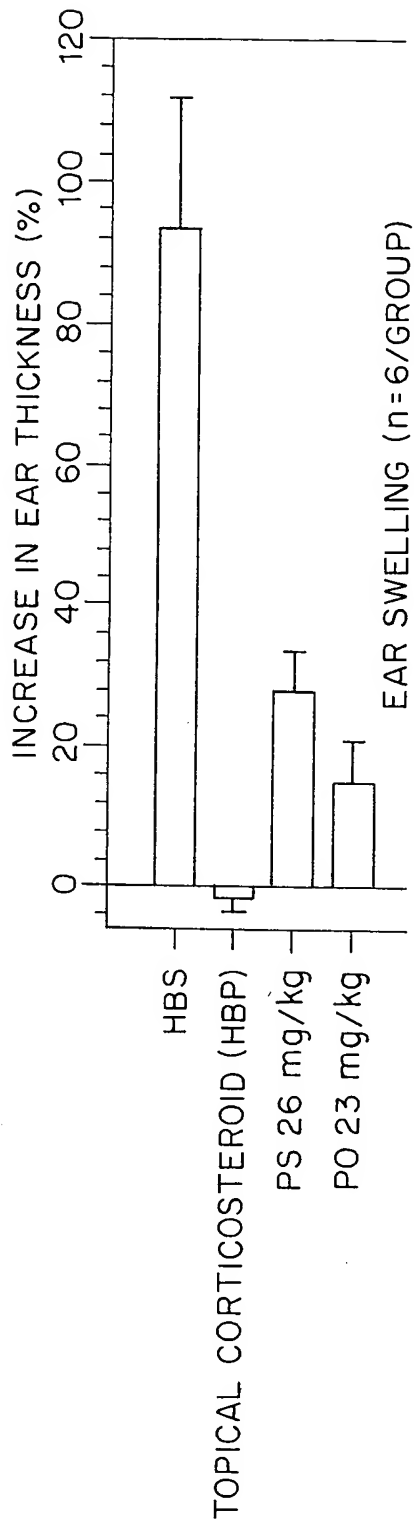


FIG. 21

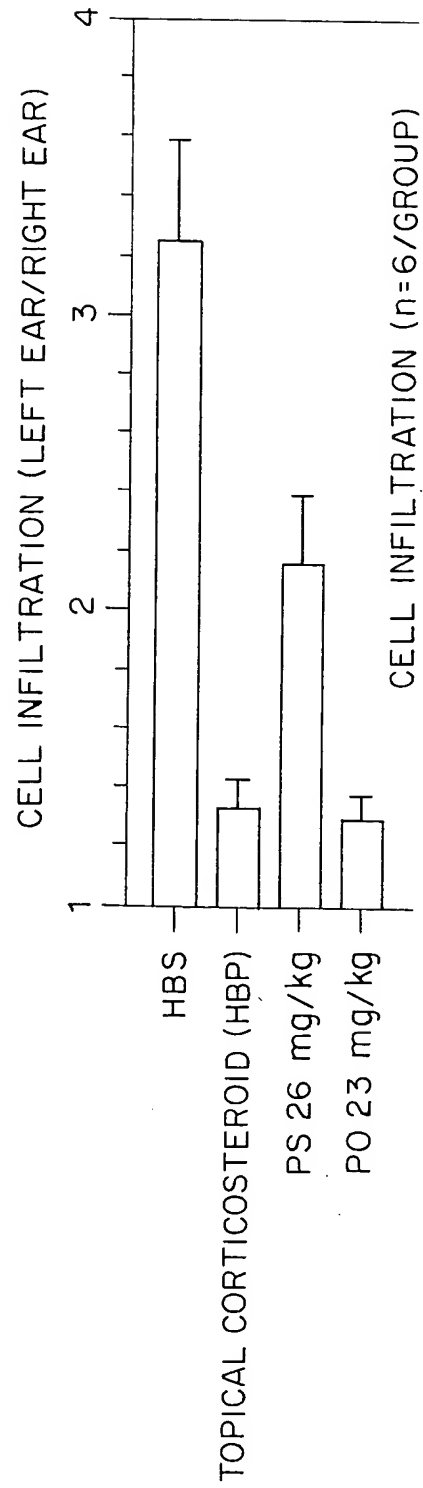


FIG. 22

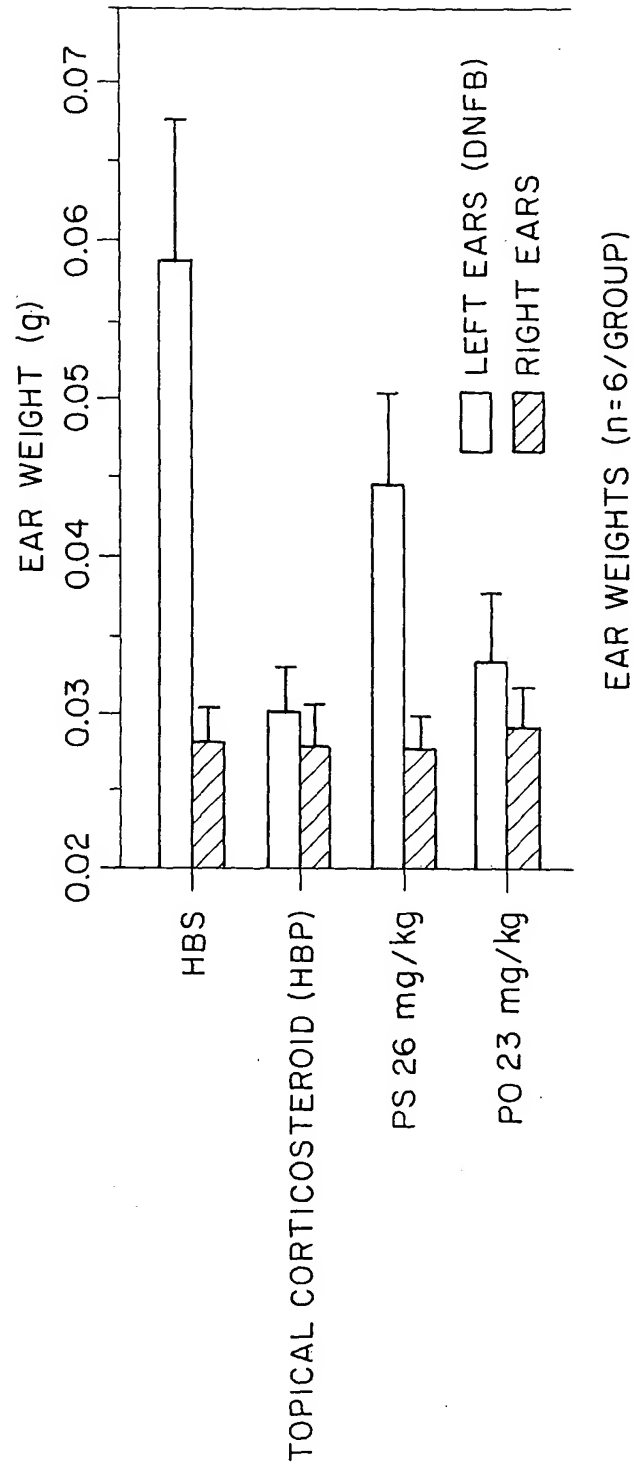


FIG. 23